

REMARKS

Claims 15, 17-23 and 25 are pending. Independent claims 15 and 23 have been amended to more clearly define the invention. First, claims 15 and 23 have been amended to recite that the growth of Lactobacillus is allowed in the vaginal area in order to overcome the objection in the Office Action which notes that the growth of Lactobacillus is affected to a certain degree at 25 ppm. The pH limitation has also been amended in claims 15 and 23 to state "acidic" rather than "in the range of 4.5 to 5.0".

The claims have been rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The Office Action states that "one skilled in the art would not recognize the hop acids at a concentration of 0.2-25 ppm would prevent growth of lactobacilli species at pH 4.5-5.0."

Independent claims 15 and 23 have been amended to state a pH of "acidic" rather than a pH "in the range of 4.5 to 5.0". The data in Table 2 shows the testing of the hop acids against lactobacilli species at pH 6.3 which meets the "acidic" limitation. Furthermore, attached is an excerpt from U.S. Patent No. 6,710,220 B2 which states at column 1, lines 20-29 that the vaginal pH may rise above 4.5-5.0 during menstruation. Thus, the testing at pH 6.3 in Table 2 does demonstrate that the recited hop acids allow growth of lactobacilli species at a pH that will be experienced in the vagina.

In *Purdue Pharma L.P. v. Faulding Inc.*, 230 F.3d 1320 (2000), the Court of Appeals for the Federal Circuit outlined the written description requirement as follows:

"In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide *in haec verba* support for the claimed subject matter at issue. See *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1570, 39 USPQ2d 1895, 1904 (Fed.Cir.1996). Nonetheless, the disclosure must ... convey with

reasonable clarity to those skilled in the art that ... [the inventor] was in possession of the invention. *Vas-Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Fed.Cir.1991). Put another way, one skilled in the art, reading the original disclosure, must immediately discern the limitation at issue in the claims. *Waldemar Link GmbH & Co. v. Osteonics Corp.*, 32 F.3d 556, 558, 31 USPQ2d 1855, 1857 (Fed.Cir.1994)."

It is respectfully submitted that the Applicant has met the written description requirement as one skilled in the art would be able to immediately discern the limitations at issue in the claims.

Conclusion

The Applicants respectfully submit independent claims 15 and 23 (and claims 17-22 and 25 that depend thereon) are in condition for allowance. Favorable reconsideration is respectfully requested.

A sheet is attached for the three month extension. No other fees are believed to be needed for this amendment. If fees are needed, please charge them to Deposit Account 17-0055.

Respectfully submitted,

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US 6,710,220 B2

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**PH REDUCING FORMULATION AND
DELIVERY SYSTEM FOR A TAMPON****FIELD OF THE INVENTION**

This invention relates to a pH-reducing formulation, an active agent delivery system and a tampon comprising the same.

BACKGROUND OF THE INVENTION

The normal, healthy human vagina is weakly acidic and has a pH of approximately 4.5. This acid condition of the vagina provides an effective barrier against the growth of pathogenic microorganisms normally associated with vaginal infection, because such microorganisms do not grow below a pH of about 5. If, however, the pH of the vagina becomes less acidic, i.e., higher than about 5, pathogenic microorganisms tend to multiply.

A change in pH of the vagina from the normal of about 4.5 to 5 to a more alkaline pH may be brought about by various vaginal conditions and may occur at any time during the menstrual cycle. During menstruation, in particular, the vagina becomes less acidic due to the presence of menstrual fluid which has a pH of from about 7 to 8. As a result, the protective barrier provided by the normal acidic condition of the vagina becomes less effective, thereby providing an environment favorable to the growth of the pathogenic microorganisms.

To overcome the reduction in acidity of the vagina and to reestablish the desired normal acidic condition, different formulations and techniques have been developed. Such efforts have included the development of formulations such as solutions, jellies, powders, suppositories, and the like containing acidifying materials which are introduced into the vagina in their prepared form.

While the above-mentioned types of products have met with acceptance, they are subject to numerous disadvantages. The solutions, jellies, powders, and suppositories containing acidifying materials may be inconvenient to handle and apply and are not fully retained in the vagina and tend to escape. In addition, they do not have capacity for absorbing vaginal fluid which may be present in the vagina, particularly during menstruation. Therefore, to use such products during menstruation, it is also necessary to use at the same time a catamenial tampon or similar article.

Other attempts to lower the pH have included physically incorporating acidifying materials into absorbent products by coating, spraying, impregnating and the like, to impart to such products acidifying properties.

U.S. Pat. No. 4,431,427 to Lefren et al, discloses a tampon having incorporated therein one or more organic acids in combination with at least one of oligomer and polymer derivatives of the acids. The acids may be citric, glycolic, malic, tartaric or lactic acid. The tampon is intended for maintaining a pH of about 4.5 to 2.5 in the fluids absorbed by the tampon during use, thereby inhibiting the growth of pathogenic bacteria in the tampon.

U.S. Pat. No. 4,661,101 to Sustmann discloses a catamenial tampon comprising a microbistatic fibrous absorbent core and an outer covering layer of a pH-regulating fibrous, cell lose material. The cellulose fibers are modified by carboxymethyl groups which are converted into their free acid form by treatment with an acid.

WO 91/08726 discloses a disposable sanitary napkin comprising a water permeable topsheet, an absorbent core

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and a water impermeable backsheet. The topsheet and/or backsheet comprise absorbable, hydrolyzable and biodegradable substances such as a lactic acid-based or glycolic acid-based polyester. This enhances the disposability of the napkin.

U.S. Pat. No. 6,020,453 to Larsson et al, discloses an absorbent article having a surface material, wherein the surface material includes a surface layer (being the outermost layer) which comprises a lactic acid-based polyester. The surface material is capable of excreting lactic acid to the surrounding urogenital region of menstruating women so as to establish a pH value of at most 4.0. The polyester has a molecular weight of at most 50,000 and the monomer/oligomer concentration is 5-30% by weight.

SUMMARY OF THE INVENTION

It is an object of the present invention to provide a novel formulation capable of reducing the pH in the menstruating vagina and/or in the tampon.

It is a further object of the invention to provide a novel delivery system for use with a feminine hygienic product, such as a tampon, to deliver an active agent to the female urogenital tract.

In a first aspect, the present invention provides a formulation effective in reducing the pH in a menstruating vagina or in a tampon inserted therein to below pH 5.5 comprising:

- (a) 3-80% by weight of a solid organic acid polymer;
- (b) 92-15% by weight of a solid organic acid; and
- (c) 5-30% of a wetting agent.

The formulation of the invention is believed to be effective in reducing the pH to below pH 5.5 in a vagina during menstruation and/or in a tampon inserted therein, and more preferably below pH 5.0, within a reasonable amount of time, such as within 0.5 hour. The components of the formulation are:

- (a) an organic acid polymer which contributes to the long-term pH reduction;
- (b) a solid organic acid which contributes to the immediate pH reduction; and
- (c) a wetting agent for facilitating release of the organic acids.

The organic acid polymer of the formulation includes two or more monomers and is primarily non-acidic prior to hydrolysis. Examples of organic acid polymers include polylactic acid, polyglycolic acid and polymalic acid or copolymers of the above. A preferred organic acid polymer in the formulation of the invention is a polymer of lactic acid. Preferred polymers are L-lactide or DL-lactide (LD), a racemic mixture of a cyclic dimer of lactic acid, and polylactic acid (PLA) in the general range of 200-2000 MW. The organic acid polymer comprises 3-80% of the formulation, preferably 60-80%, most preferably 70-80%.

Examples of solid organic acids are citric, malic, maleic, fumaric, succinic, tartaric and oxalic acids. A preferred organic acid is citric acid. The organic acid comprises 92-15% of the formulation, and preferably 30-15%.

Examples of wetting agents which may be used in the formulation of the invention include glycerol, polyethylene glycol (PEG), polypropylene glycol (PPG) and surfactants with an HLB ranging from 10 to 18. Preferred wetting agents are glycerol and PEG-8000. The wetting agent comprises 5-30% of the formulation, and preferably 5-10%.

The formulation may comprise additional substances such as stabilizers, perfuming agents, preservatives, anti-oxidants, chelating agents, adsorbents, analgesic agents, anti-inflammatory agents, etc.